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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/702,878	11/01/2000	Hiroshi Tamura	159-62	3533

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/702,878	Applicant(s) TAMURA ET AL.	
	Examiner Lisa V. Cook	Art Unit 1641	

-- Th MAILING DATE of this communication appears on the cov r sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. Applicant's response to the office action mailed 09 April 2003 is acknowledged. In amendment-B filed therein claims 1-9 were canceled without prejudice. New claims 10-23 were added. Currently claims 10-23 are pending and under consideration.

Election/Restrictions

2. Applicant's request for reconsideration of the restriction requirement is Moot because claims 1-9 have been canceled without prejudice.

OBJECTIONS WITHDRAWN

Priority

3. If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed copending application, specific reference to the earlier filed application (55352/1999-filed 3/3/1999 in Japan) must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph.

Applicant has amended the specification to cross reference the Japanese priority document. Accordingly the objection is withdrawn.

Information Disclosure Statement

4. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

5. The information disclosure statements filed 11/01/01 - Paper#2, filed 1/30/01 – Paper #4, filed 7/11/01 – Paper #5, and filed 9/30/02 – Paper #9 have been considered as to the merits prior to First Action.

Applicant has indicated reference duplication in the PTO-1449 forms executed 3/24/03 and 4/26/03. Examiner has checked and indicated the appropriate duplicate references. The objection is withdrawn.

Specification

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

I. The use of the trademarks has been noted in this application. (See for example "Xenon" page 12 line 6, "Fisher" page 17 line 13, "Triton" page 18 line 5). They should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Applicant has amended or addressed the cited trademarks. Accordingly the objection is withdrawn.

II. Abstract - Applicant is reminded of the proper language and format for an abstract of the disclosure. The instant Abstract uses the term "relates". "The subject invention "relates" to. Please correct.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

Applicant new abstract submitted 10/9/03 has obviated the objection to the abstract.

Claim Rejections

7. The rejections of claims 1-2 and 4-7 under 35 USC § 112, 35 USC § 102, and 35 USC § 103 are of record in paper #10. The rejections are MOOT because the claims have been canceled without prejudice.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 10-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 10 and 17 are vague and indefinite because it is not clear as to how the concentration of CRP will be measured if the control solution containing known concentrations of CRP is not included in the assay procedure. As recited the claims recite the reaction of a sample "or" a control solution. See claim 10 step (ii) and claim 17 line 4. This is also a problem because the final determination of CRP concentration is compared with that of the control. It is not clear how this analysis is possible if the control solution is not assayed in the previous steps. It is suggested that the method include separate steps for analyzing the sample and the control solution for clarity.

B. The term "immobilizing phase" in claim 10 is a relative term, which renders the claim indefinite. The term "phase" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claims are directed to the immobilization of a formed binding complex, however "phase" is not clear. Is it applicant's intent to mean a solid support, a solution, or some other embodiment? Appropriate correction is required.

C. In claim 20 the requirement that the label comprise both radioactive and non-radioactive material is ambiguous. The label cannot be both simultaneously. The claim should be worded to read on only one in order to obviate this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 17-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for assays that include an immobilized complex which is separated from unbound material, it does not reasonably provide enablement for reactions including multiple reagents which form a complex that can be separated from unbound materials with out immobilization. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The disclosure teaches immobilization, allowing for bound and unbound complex separation in examples beginning on page 17 line 24. A solid support (tubes, micro titer plate/well, resin, gel, pellet formation, etc) is needed to collect the bound materials for analysis. Without the support all the materials will remain in solution and cannot be separated. Accordingly the method recited in claims 17-23 is not enabled.

Please Note: With respect to the art rejections claims 17-23 have been interpreted as having a broad scope not reciting the immobilizing step and therefore read on the cited art wherein immobilization techniques are included.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

I. Claims 10-13 and 17-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Heggli (GB 2 217 335 A).

Heggli disclose a method of measuring CRP (c reactive protein) via binding to phosphoryl choline (PC) residues and/or aminoethyl dihydrogen phosphate (AEDP). See abstract and claims.

Enzymes labeled with PC or AEDP are employed to generate a detectable measurement indicative of the bound CRP. See page 6. The method was tested on serum and plasma samples. Page 3. The reference teaches the utility of antibodies to CRP (anti-CRP) as ligands in assay methods. Page 3 lines 16-24. In one embodiment a CRP-binding membrane (anti-CRP immobilizing phase) is added to a test sample (sample solution) and the bound CRP is quantitatively or qualitatively detected by a second CRP-binding signal substance. Page 5 lines 33-36. Enzymes labeled with PC or AEDP residues, or antibodies to CRP are used to give a measurable colored solution. The change in light intensity is directly proportional to the amount of bound CRP. See page 6.

Although the reference is silent with respect to signal comparison with a control, this is viewed as an inherent property of assay systems. Control comparisons are performed to account for signal background and increase assay precision and accuracy. A claim is anticipated if each element of the claim is found, either expressly described or under principles of inherency, in a single prior art reference, or that the claimed invention was previously known or embodied in a single prior art device or practice.

Response to Argument

Applicant contends that Heggli fails to teach the use of a labeled phosphorylcholine component. This argument was carefully considered but not found persuasive because Heggli et al. employ enzyme labeled phosphorylcholine (PC) residues to measure CRP. Please see abstract and page 6.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 10-13 and 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siboo et al. (Journal of Immunological Methods, 23, 1978, pages 59-67) in view of Robey et al.(The Journal of Biological Chemistry, Vol258, No63/25/83, pages 3895-3900).

Siboo et al. disclose a fluorescent binding immunoassay to measure C-reactive protein (CRP) in human and mouse sera (serum). See abstract. Anti-CRP immobilized on micro spheres (RGAHCRP) is added to known concentrations of human CRP. A bound complex was formed and after separation of bound and un-bound materials, a second anti-CRP labeled complex was added to bind the formed complex.

The second anti-CRP is conjugated to the label fluorescein. The bound measurement was compared to controls (RGAHCRP-micro beads and RGAHCRP-F without HCRP). See page 61 2nd paragraph. This assay was also conducted on normal and pathological human and mouse sera. See page 62 2nd paragraph.

Siboo et al. differ from the instant invention in not specifically teaching the utility of a labeled phosphorylcholine in place of the second anti-CRP conjugated to fluorescein in order to measure C-reactive protein.

However, Robey et al. teach this limitation. Labeled derivatives of phosphorylcholine were synthesized and used in C-reactive binding studies. The interaction of C-reactive protein and labeled phosphorylcholine was measured by electron spin resonance spectrometry. See abstract, page 3896 – 2nd column – 2nd paragraph, and page 3897 –Results.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize labeled phosphorylcholine derivatives in C-reactive binding protein reactions because Robey et al. taught that "the spin labeled phosphorylcholine derivatives [also] rival phosphorylcholine as a ligand for the human, dog, and *Limulus* C-reactive proteins. The use of known labeling ligands to CRP is deemed mere optimization. It would have been obvious to replace the tag employed by Siboo et at. (second anti-CRP conjugated to fluorescein) with the labeled phosphorylcholine taught by Robey et al. as a means for optimizing the assay. Absent evidence to the contrary one of ordinary skill in the art would have employed labeled phosphorylcholine as a ligand to C-reactive protein, such modifications are routinely performed in assay systems to maximize data results.

II. Claims 14-16 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heggli (GB 2 217 335 A) in view of Hemmila et al. (Analytical Biochemistry, 137, 335-343, 1984).

Please see Heggli as set forth above.

Heggli differ from the instant invention in failing to teach Eu as the label to PC.

However, Hemmila et al. teach europium as a label in time-resolved immunofluormetric assays/method. See abstract. The lanthanide, europium(III) is taught to form highly fluorescent chelates with many different organic ligands. The lanthanide has been used a fluorescent probes in the study of Ca-binding sites enzymes, proteins, and in the measuring of nucleic acid conformation. See pages 335, 1st column. In this study europium was detected and quantified after an immunoreaction. Page 336, 1st paragraph. Europium could be utilized as the labels with an antibody, antigen, or hapten. See page 342, 1st column 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a europium compound as taught by Hemmila et al. to label PC in the CRP-PC binding assay/methods of Heggli because Hemmila et al taught that the long fluorescent decay time of the label (europium) makes it suitable as a label in the measurement of biospecific affinity reactions. Further the use of europium as a label in time-resolved fluoroimmunoassays makes it possible to achieve highly sensitive measurements, which incorporate the positive features of FIA but avoid the drawbacks of RIA. Page 335 2nd column. Further the europium label is stable, involves no radioactivity, and requires a counting time of only 1 second. See page 342, last paragraph.

III. Claims 14-16 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Siboo et al. (Journal of Immunological Methods, 23, 1978, pages 59-67) in view of Robey et al.(The Journal of Biological Chemistry, Vol258, No63/25/83, pages 3895-3900) and in further view of Hemmila et al. (Analytical Biochemistry, 137, 335-343, 1984).

Please see Siboo et al. in view of Robey et al. as set forth above.

Siboo et al. in view of Robey et al. differ from the instant invention in failing to teach Eu as the label to PC.

However, Hemmila et al. teach europium as a label in time-resolved immunofluormetric assays/method. See abstract. The lanthanide, europium(III) is taught to form highly fluorescent chelates with many different organic ligands. The lanthanide has been used a fluorescent probes in the study of Ca-binding sites enzymes, proteins, and in the measuring of nucleic acid conformation. See pages 335, 1st column.

In this study europium was detected and quantified after an immunoreaction. Page 336, 1st paragraph. Europium could be utilized as the labels with an antibody, antigen, or hapten. See page 342, 1st column 3rd paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a europium compound as taught by Hemmila et al. to label PC in the CRP-PC binding assay/methods of Siboo et al. in view of Robey et al. because Hemmila et al taught that the long fluorescent decay time of the label (europium) makes it suitable as a label in the measurement of biospecific affinity reactions.

Further the use of europium as a label in time-resolved fluoroimmunoassays makes it possible to achieve highly sensitive measurements, which incorporate the positive features of FIA but avoid the drawbacks of RIA. Page 335 2nd column. Further the europium label is stable, involves no radioactivity, and requires a counting time of only 1 second. See page 342, last paragraph.

Response to Arguments

Applicant contends that the primary references did not teach the invention and Hemmila et al. does not cure the deficiencies of the primary references. The response to the primary reference of Heggli et al. is set forth above. While new references of Siboo et al. in view of Robey et al. have been cited.

12. For reasons aforementioned, no claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

14. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Kishida et al. (Ensho, 1989, ((5), 369-74 Abstract Only) teach a method of evaluating the binding specificity of Human C-reactive protein and phosphorycholine with affinity chromatography.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The official Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to send an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 305-3399.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Lisa V. Cook
CM1-7B17
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1/8/04

LONG V. LE
SUPERVISORY PATENT EXAMINER
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